REMARKS/ARGUMENTS

Claims 1-16 and 33-36 are pending in this application. Claims 17-32 and 37-40 were previously canceled.

I. Rejections under 35 U.S.C. 112

Claims 1-6, 8-16 and 33-36 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in a way that would convey to those skilled in the art that the inventor had possession of the claimed invention. Applicant respectfully traverses this rejection because the Office Action erroneously concludes that Applicant was not in possession of the full scope of the genus of coupling agents having a pKa ranging from about 3.3 to about 4.5 that are used in the claimed invention.

Specifically, the Office Action improperly applies the *Guidelines for Examination of Patent Applications Under the 35 USC 112, paragraph 1, Written Description Requirement* (Fed. Reg., Vol. 66, No. 4, pages 1099-1111, Jan. 5, 2001) ("the Guidelines") and, as a result, erroneously concludes that Applicant's claimed invention should be limited to the use of 5-(ethylthio)-1*H*-tetrazole as the *sole* coupling agent in carrying out the methods of the claimed invention. The Office Action, for example, is mistaken with respect to its assertion that compliance with the written description requirement can only be established for a claimed genus by exemplification of a representative number of species,. The Guidelines actually provide that this requirement may be met in various ways:

> (2) For each claim drawn to a genus:
>
> The written description requirement for a claimed genus **may** be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a), above), reduction to drawings (see (1)(b), above), **or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient**

> **to show the applicant was in possession of the claimed genus** (see (1)(c), above).
>
> [page 1106, column 3, lines 12-29, emphasis supplied, attached hereto as Exhibit A]

It is clear from the emphasized portion of the Guidelines that written description for a claimed genus **may also** be provided by: disclosure of relevant, identifying characteristics, *i.e.,* structure or other physical and/or chemical properties; disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure; or disclosure of a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Here, Applicant readily identifies the characteristics of the coupling agent in terms of a well-recognized physical / chemical property, the pKa, and discloses the correlation between pKa and the resulting enantiometric ratio. Applicant has found that the pKa of the coupling agent influences the enantiomeric ratio of Sp to Rp linkages when the coupling agents are used in the methods of the present invention (page 8, lines 8-13). The specification provides that a pKa below about 3.3 would cause removal of the protecting group at the 5'-hydroxyl position of the incoming 2'-substituted nucleoside (page 25, lines 19-20). Furthermore, Table 10 (page 26) presents data comparing the coupling agents, 5-(ethylthio)-1H-tetrazole (ETT), 1H-tetrazole (1H-T), pyridium trifluoroacetate (PTFA), 4,5-dicyanoimidazole (DCI), and imidazolium triflate (ImTf). The provided data indicate that a pKa ranging from about 4.8 to about 5.5 does not significantly influence the stereochemical outcome of the phosphorothioate linkage.

In reporting these findings, Applicant clearly discloses that coupling agents having a pKa ranging from about 3.3 to about 4.5 provide internucleotide linkages enriched in the Sp enantiomer. Moreover, the specification (page 9, lines 1-3) teaches that the pKa of suitable coupling agents can be determined using well known methods in the art, such as potentiometric titrations, that are provided in Cookson, R. F. Chemical Reviews, Vol. 74, No. 1, page 5 (1972).

Because the claimed genus of coupling agents having a pKa ranging from about 3.3 to about 4.5 is indeed described in the specification in a way that would convey to those skilled

in the art that they had possession of the claimed invention, the instant rejection under § 112, first paragraph, is improper and should be withdrawn.

II. Objections to the Claims

The Office Action objects to claim 7 as being dependent upon a rejected base claim, but indicates that the claim would be allowable if rewritten in independent form. Applicant respectfully submits that the objection to claim 7, which is dependent to claim 1, is improper in view of Applicant's remarks made above.

III. Conclusions

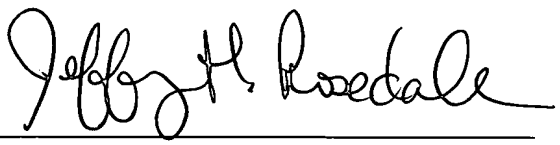
Applicant requests the Examiner to:

(1) reconsider and withdraw the standing rejections of the claims; and

(2) pass claims 1-16 and 33-36 to allowance.

If the Examiner is of contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-5984.

Respectfully submitted,



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